MSCBMP2880 - Cellular Biology of Normal and Disease States

Course Director:

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Focus of the class:

The course is broadly divided in to two sections. In the first section of the course, leading up to the mid-term exam, the students will primarily explore subcellular protein and lipid trafficking. The topics include the fundamentals of protein folding followed by the trafficking of proteins through the endoplasmic reticulum and Golgi on their way to their correct destinations in the apical or basolateral membranes of epithelia. There are additional lectures dedicated to the chaperones that aid in the folding of proteins as well as to what happens when these proteins are incorrectly or mis-folded, the posttranslational modifications that ensue and their ultimate targeting to the proteasome for degradation. The role of posttranslational modifications will be further explored as it relates to progression through the cell cycle and its role in cancer. Finally, cell-cell contacts will be explored as well as their breakdown during cell migration.

In the second section of the course, leading up to the final exam, the students will primarily explore topics at the cellular level. A key aspect of cellular function is the transcellular movement of ions and nutrient molecules and this will be explored in a series of lectures. Additional lectures will focus on the mechanisms by which viruses co-opt the cellular machinery, covered in the first half of the course, to invade the cell undetected. Subsequently, the cell biology of ageing and senescence will be explored followed by a discussion of the role of mitochondria in health and disease. Finally, the course will close with lectures on the role of microRNAs in physiology.

In each series of lectures, both the normal cell biology as well as how disruption in these processes ultimately leads to disease will be covered. At the end of the course students will have an increased understanding of normal cellular function and how research in cell biology can lead to a deeper understanding of diseases that impact millions of people each year.

Meeting times and place:

Class meets on Tuesdays and Thursdays from 10:30-12:30 in the Cell Biology conference room (BSTWR-S373) Jan 7th through April 25th with the exception of Monday, January 11th. Classes will not be held on March 8th and 10th due to spring break.

Structure of the course:

The course consists of both didactic lectures as well as a review of seminal papers in the fields being discussed as a means of both supporting the information provided in the lectures as well as providing additional primary data that is discussed in detail as to the methodologies, the hypothesis generated and the way in which these data support the conclusions of the manuscript. It is important that the students have read the manuscripts before class so that they can contribute to the discussion by asking questions concerning the methods, hypothesis and conclusions. Of course, it is also anticipated that the students will actively participate during the didactic lectures. A dynamic exchange of ideas coupled with probative questions is always the best way to learn while also making the classroom a more exciting place for both the students and faculty.

How you will be evaluated:

You will be evaluated based on your scores on two written take-home examinations.

Take-home exams will be distributed at approximately the middle of the course and at the end of the course. You will have 6-7 days to complete your exams. The completed exams (as a ©Word or pdf file format), must be returned to Sarah Biancardi at sab181@pitt.edu by 4PM on the due date. Exams received after 4PM on the due date will be scored with a 10% penalty (i.e. a score of 90% will be decreased to 80%). If there is a compelling reason that an exam must be submitted after the due date the

student should contact the course director at dd2@pitt.edu to explain their rationale and get permission for a late submission.

In general, exam questions will ask you to take the information you have learned in class and extrapolate this to answer a broader question in the field of cell biology. In some cases, this will include the appropriate design of experiments to answer a question, whereas in other cases you will be expected to take what you have learned in class and apply this to a unique question. You can use any classroom materials and relevant outside sources, as required. However, you are expected to work alone, to develop your own ideas, and to remember the following:

1. You may not cut-and paste any sentences, paragraphs, figures or other information directly from published sources. This constitutes plagiarism.

2. All citations of published as well as unpublished sources (e.g. web sites and personal communications) must be comprehensive.

COURSE SCHEDULE:

January 7: Protein Synthesis and Folding 1 – Thibodeau

January 11: Protein Synthesis and Folding 2 – Thibodeau
(CHANGE IN SCHEDULE)

January 14: Cargo selection in the ER 1 - Aridor
January 19: Cargo selection in the ER 2 - Aridor

January 21: ERAD, ubiquitylation, proteasomal degradation – Guerriero/Ninehouser
January 26: Chaperones and folding – Guerriero/Ninehouser

January 28: Journal presentation – Guerriero/Ninehouser
February 2: Epithelial polarity and cancer – Y. Hong

February 4: Epithelial polarity and cancer – Y. Hong
February 9: Membrane homeostasis and lipid sorting 1 – Hammond

February 11: Membrane homeostasis and lipid sorting 2 – Hammond
February 16: The Metazoan experience: adhesion complexes, cellular organization and tissue integrity – Kwiatkowski

February 18: Life at the leading edge: regulated cell movement – Kwiatkowski
February 23: PTM and cell cycle – Wan

February 25: Cell Cycle and cancer treatment based on PTM – Wan
Hand out Mid-Term Exam

March 1: Fundamentals of Ion Transport – Devor

March 3: Chloride secretion, CF and Cholera – Devor
Mid-Term exam due by 4 p.m.

Spring Break March 8 and 10

March 15: Sodium transport in the kidney – Subramanya
March 17: Endocytosis, Recycling and Degradation of ion transporters – Subramanya

March 22: Routes and mechanisms of viral entry into the cell – Thorne
March 24: Viral co-opting of cellular processes – Thorne

March 29: Autophagy and Cell Death – Lamitina

Papers:

Baker DJ, Wijshake T, Tchkonia T, LeBrasseur NK, Childs BG, van de Sluis B, Kirkland JL, van Deursen JM. Clearance of p16Ink4a-positive senescent cells delays ageing-associated disorders. Nature. 2011 Nov 2;479(7372):232-6. doi: 10.1038/nature10600.

Martinez-Lopez N, Garcia-Macia M, Sahu S, Athonvarangkul D, Liebling E, Merlo P, Cecconi F, Schwartz GJ, Singh R. Autophagy in the CNS and periphery coordinate lipophagy and lipolysis in the brown adipose tissue and liver. Cell Metabolism 2015 (in-press).

March 31: Ageing and Senescence –Lamitina

April 5: Journal presentation – Lamitina

Review: Baker DJ, Wijshake T, Tchkonia T, LeBrasseur NK, Childs BG, van de Sluis B, Kirkland JL, van Deursen JM. Clearance of p16Ink4a-positive senescent cells delays ageing-associated disorders. Nature. 2011 Nov 2;479(7372):232-6. doi: 10.1038/nature10600.

Review: Martinez-Lopez N, Garcia-Macia M, Sahu S, Athonvarangkul D, Liebling E, Merlo P, Cecconi F, Schwartz GJ, Singh R. Autophagy in the CNS and periphery coordinate lipophagy and lipolysis in the brown adipose tissue and liver. Cell Metabolism 2015 (in-press).

April 7: Mitochondrial fusion and fission - Goetzman

April 12: Mitochondrial function in health/disease - Goetzman
April 14: The role of microRNAs in normal development, physiology and cell biology - Butterworth

April 19 : MicroRNAs and disease –Butterworth
Hand Out Final Exam
April 21: No class

April 25 (Monday): **Final Exam due by 4 p.m.** – No Class